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Book Reviews

The Enzymes, Volume 19: Mechanisms of Catalysis, 3rd Edition; Edited by D.S. Sigman and P.D. Boyer; Academic Press, San Diego, 1990; ix + 459 pages; $99.00

When I started preparing this review I thought that Paul Boyer's excellent series was so well known that it was hardly necessary to bring it to the attention of librarians and the biochemical public, though some account of the particular chapters in the volume might be useful. However, when I had occasion last month to refer to an article in volume 17, I was astonished to discover that none of the five science libraries in Marseilles that I approached possessed a copy, and none of the librarians had heard of the series! So let me take the occasion of Paul Boyer's retirement from the editorship as an opportunity to recognize the service that he has done to the community over many years of editing *The Enzymes*.

Volume 19 is in many respects a return from the specificity of recent volumes to the broader view of volumes 1 and 2. As these were published more than twenty years ago this is very welcome. It does not entirely replace these volumes, but it extends them in major ways, taking account of the great advances in knowledge that have occurred, and adding areas of the subject that hardly existed when the present edition started, such as site-directed mutagenesis (K.A. Johnson and S.J. Benkovic), suicide inactivation (M.A. Ator and P.R. Ortiz de Montellano), and site-specific modification (R.F. Colman). Other topics, such as the relationship between binding energy and catalysis (D.B. Hackney), electron transfer (D.C. Rees and D. Farrelly) and stereochemistry of reactions at carbon (D.J. Creighton and N.S.R.K. Murthy), are now understood so much better that a revised account was needed.

Rather than try to cover all of these superficially, I shall discuss the chapter on site-directed mutagenesis in more detail, as its standard can be regarded as representative of the volume as a whole. The newness of the subject is illustrated by the fact that of nearly 160 references only three are to work published before volume 1 of the series, and the great majority date from the last five years. The major sections deal with the structural effects of mutation, the effects on substrate binding and catalysis, and the possibilities of engineering new specificities or functions. Perhaps the most important point brought out in the chapter is the need for studies in site-directed mutagenesis to be well grounded in classical enzymology and protein structure. Random or arbitrary amino-acid substitutions rarely lead to much advance in understanding the functioning of an enzyme, but carefully selected and analysed changes can reveal a great deal. As the authors remark in the context of mutant subtilisins, there are few surprises in the variations in properties that are found, but, at least in part, their lack of surprise results from their approaching the subject not as a fashionable novelty but as a natural development from the study of chemical mechanisms and kinetics.

Although in general I find this chapter excellent, I have to comment on a logical fallacy that illustrates the danger of using a mathematical argument to make a point that can be understood more simply in other ways. Noting that the sequences of two proteins of 100 residues each can be regarded as two points in a surface composed of 10^{130} points, Johnson and Benkovic claim that the high dimensionality 'results in a large number of paths between any two structures and ensures that at least some of the paths and intermediate structures between the two points will be allowed'. I take this to mean that the vastness of the number of routes that can be conceived for converting, for example, human cytochrome *c* into *Candida krusei* cytochrome *c* by single-residue substitutions, deletions or insertions requires the existence of a route such that every intermediate structure represents a functional protein. Whether the conclusion is true or not, it does not follow from this argument. If I were to claim that the equally high dimensionality of the surface containing the two sentences 'in recent years directed mutagenesis has become a useful method of studying enzyme function' and 'the function of enzymes can now be investigated by directed mutagenesis with useful results' (each contain 91 letters and spaces, 27^{91} is similar in magnitude to 20^{100}) ensures that one can convert one to the other by one-letter mutations such that each intermediate sentence is meaningful, most readers would ignore the arithmetic and ask how it was done. When the underlying constraints are unknown one is more likely to accept a mathematical argument uncritically. However, this is a minor point in a generally excellent chapter, typical of a volume that should be available to any serious researcher in modern enzymology, a volume well worthy of Paul Boyer.

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